

promising new insecticide dieldrin (497) under field conditions, tests involving treatment of approximately 330 blocks were initiated at the Phoenix project in August 1949. To date the results have been promising, but are as yet inconclusive.

Investigations on the overwintering habits of

flies were begun during the winter of 1949-50. Future plans include expanding these investigations and initiating others on the developmental cycles, breeding habitats, and the daily activities of the prevalent domestic flies in each of the cities.

Virus Encephalitis in the Missouri River Basin

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The arthropod-borne virus encephalitides include the well recognized entities of Eastern, Western, and Venezuelan equine encephalomyelitis and St. Louis, Japanese B, and Russian Far East encephalitis. Other new viruses, the importance of which is still not clearly defined, are constantly being discovered in various parts of the world, among them being those of West Nile, Semlike Forest, Bwamba Forest, Bunyamwera Ilheus, and California.

Although widespread infections of equines involving the central nervous system have occurred repeatedly in many parts of the United States since the early part of the nineteenth century, the etiology of such epizootics or plagues remained unknown until Meyer, Haring, and Howitt (1) isolated a virus (Western encephalomyelitis strain) from equine brain tissue in 1930. The identification of an Eastern strain as distinct from that of the Western one was made in 1933 by TenBroeck and Merrill (2). The possibility that human disease may be caused by the equine viruses was suggested by Meyer in 1932 (3), but it was not until 1938 that Howitt (4) recovered the Western strain and Webster and Wright (5) the Eastern strain from human cases. In 1933, a sharp epidemic of about three thousand human cases of an unknown encephalitis occurred primarily in the city and county of St. Louis, Mo. It quickly was shown that this outbreak was due to a neurotropic virus which is now identi-

fied as the St. Louis strain. In 1945, Hammon *et al.* (6) isolated what may be a new strain from mosquitoes in California. This is known tentatively as the California strain, and serum from a child suffering from encephalitis gave significant serological reactions to it (7). The first clue to the method of spread of these viruses was provided by Kelser in 1932 (8) when he demonstrated that *Aedes aegypti* mosquitoes could transmit an equine encephalomyelitis virus from infected guinea pigs to susceptible ones. Following this lead, the work of other investigators showed that a relatively large number of arthropods can pass the virus to susceptible animals under laboratory conditions. It was not until 1941, however, that Hammon and his associates (9) recovered encephalitis virus from wild mosquitoes. Since 1941 the viruses of Western and Eastern encephalomyelitis, St. Louis encephalitis, and the California strain have been recovered from a wide range of arthropods, many of which have been shown to be capable of passing the virus from one vertebrate to another under laboratory conditions. Furthermore, indications of infection with these strains have been found in birds and mammals, and the serological data would indicate that these infections are rather common occurrences. The results of major contributions with respect to possible vectors and reservoirs are summarized in table 1.

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TABLE 1
Summary of Encephalitis Virus Transmission Studies
and of Natural Infections Involving Arthropods

SPECIES	LABORATORY TRANSMISSION			NATURAL INFECTIONS			
	Eastern	Western	St. Louis	Eastern	Western	St. Louis	Others
<i>Anopheles maculipennis</i>	-	-	-		+(20)		
<i>freeborni</i>	-	-	-				
		(20, 22)					
<i>Aedes</i>							
<i>aegypti</i>	+(8, 13)	+(13)	+(21)				
<i>sollicitans</i>	+(13)	+(13)					
<i>cantator</i>	+(13)						
<i>dorsalis</i>		+(14)	+(40)		+(24)	+(40)	California (24)
<i>nigromaculis</i>		+(15)	+(21)				
<i>vexans</i>		+(16)	+(21)				
<i>albopictus</i>		+(9)					
<i>taeniorhynchus</i>		+(16)	+(21)				
<i>campestris</i>		+(9)					
<i>atropalpus</i>	+(17)						
<i>triseriatus</i>	+(17)						
<i>lateralis</i>			+(21)				
<i>Culex</i>	-	-					
<i>pipiens</i>		(13, 17, 22)	+(19)			+(20)	
<i>tarsalis</i>	+(21)		+(18)		+(9)	+(9)	California (27)
<i>salinarius</i>							
<i>coronator</i>			+(18)				
<i>stigmatosoma</i>					+(24)		
<i>restuans</i>					+(23)		
<i>Culiseta</i>							
<i>inornata</i>			+(21)		+(20)		
<i>incidens</i>			-(21)				
<i>Mansonia</i>							
<i>tittilans</i>							Venezuelan (25)
<i>perturbans</i>				+(26)			
<i>Dermacentor</i>							
<i>andersoni</i>		+(28)	+(30)				
<i>andersoni</i>			transovar- ian passage (31)				
<i>Triatoma</i>							
<i>sanguisuga</i>					+(29)		
<i>Dermanyssus</i>							
<i>gallinae</i>			+(37)		+(33)	+(32)	
<i>Liponyssus</i>			transovar- ian passage (37)		+(34)		BFS-867 strain (35)
<i>sylviarum</i>							
<i>Eomenacanthus</i>					+(37)		
<i>stramineus</i>							
<i>Liponyssus</i>							
<i>bursa</i>					+(36)		

With the exception of sporadic investigations during the more severe epidemics and epizootics, little has been done which would specifically review or point up the encephalitis problem in the Midwestern area. Present conditions and contemplated future developments in the Missouri River Basin emphasize the need for such a review. The object of this paper is to present and discuss existing data for the purpose of clarifying the status of the encephalitis problem in these 10 States: Colorado, Iowa, Kansas, Minnesota, Missouri, Montana, Nebraska, North Dakota, South Dakota, and Wyoming.

INCIDENCE IN THE MISSOURI RIVER BASIN

According to published reports, two strains of the arthropod-borne encephalitides have been identified in the States herein considered. These are Western equine encephalomyelitis and St. Louis encephalitis. Since these strains infect both horses and humans, a review of their distribution and occurrence must include equine as well as human infections.

Equine Infections. Since the etiological agent of encephalomyelitis in horses was not discovered until 1931, the incidence of equine infections prior to that time cannot be established positively. Nevertheless, the numerous reports by veterinary scientists dating from 1850 which are referred to by Meyer (3) and the Botulism Commission (11) indicate that many extensive epizootics described as "Cerebrospinal Meningitis," "Borna Disease," "Nonpurulent Encephalitis," "Forage Poisoning," "Kansas-Nebraska Horse Plague," and "Botulism" occurred during the latter part of the nineteenth century, and periodically during the twentieth century. In the opinion of many investigators, these widespread outbreaks were due, at least in part, to one or more of the encephalitis viruses. The severity of these early epizootics is emphasized in reports describing such losses as 35,000 equines in Kansas and Nebraska in 1912; 1,000 in Colorado in 1919; 17 outbreaks involving 1,004 animals in Montana in 1919, and 1,500 in South Dakota in 1918.

In 1935, the U. S. Department of Agriculture, Bureau of Animal Industry, began accumulating data on the incidence of equine encephalomyelitis infections throughout the country. During the period 1935 to 1948, approximately 495,609 cases were reported. Further analysis of these reported cases show that over 385,000, or approximately 77 percent occurred in 10 Midwestern States. Details of these data are presented in table 2 and figure 1.

TABLE 2

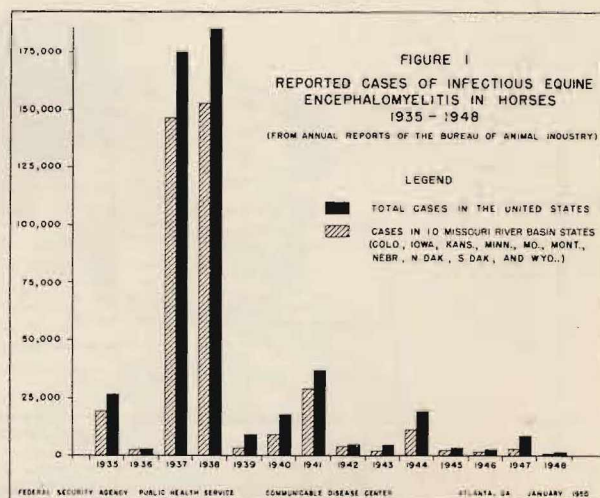
Equine Encephalomyelitis Cases Reported from the United States* and Those from 10 Midwestern States** 1935-1948

Year	United States	Midwestern States
1935	25,000***	19,980
1936	3,300***	2,926
1937	175,000***	146,587
1938	184,662	152,620
1939	8,008	3,352
1940	16,941	9,273
1941	36,872	28,899
1942	4,939	3,117
1943	4,768	1,973
1944	19,590	11,231
1945	3,212	1,442
1946	2,805	1,202
1947	8,716	2,405
1948	1,796	628
	495,609***	385,635

*U. S. Department of Agriculture Reports.

**Colorado, Iowa, Kansas, Minnesota, Missouri, Montana, Nebraska, North Dakota, South Dakota, and Wyoming.

***Approximated.



In the Midwestern area, major epizootics occurred in 1935, 1937, 1938, 1941, and 1944. During these years approximately 359,405 cases were reported. As indicated in table 3, the epizootics of 1937 and 1938 were very severe, particularly in the States of Iowa, Kansas, Minnesota, North Dakota, and South Dakota. From the tables it may also be

noted that over the country generally, and in Midwestern States as well, the total number of reported cases and the size of epizootics have gradually diminished since 1938. Many factors, such as the total number of horses, number of susceptible horses, number of vaccinations, the economic value of equines, and others must be considered in interpreting these trends.

Further analysis of the incidence of horse infections for the epizootic years 1941 and 1944 are shown on figures 2 and 3 respectively. It will be noted that the geographical area involved in the epizootic of 1941 differs somewhat from that of 1944 within the States considered. During both of these epizootics, however, the incidence in hundreds of counties distributed throughout several States was considerably above the normal rate of approximately 2 cases per 1,000 animals. Furthermore, many counties had the significantly high rate of more than 10 cases per 1,000 animals. On the same basis, a review of the reported cases for the period 1941 to 1949 was completed. This is shown on figure 4. It is evident that over this

TABLE 3
Equine Encephalomyelitis Infections
in the 10 Midwestern States
during Five Major Epizootics*

States	1935	1937	1938	1941	1944
Colorado	1,456	2,074	3,656	1,040	255
Iowa	**	31,884	66,092	5,963	2,121
Kansas	3,000	16,257	10,250	886	1,157
Minnesota	3,337	41,159	23,686	6,777	1,470
Missouri	17	4,632	10,242	8,671	4,160
Montana	111	743	13,102	167	42
Nebraska	3,400	**	13,881	1,030	1,571
N. Dakota	8,244	20,226	2,553	2,552	126
S. Dakota	115	29,702	5,203	1,304	268
Wyoming	300	**	3,955	507	61
Total	19,980	146,677	152,620	28,897	11,231
Grand Total					359,405

*U. S. Department of Agriculture and Bureau of Animal Industry Reports.
 **No data available.

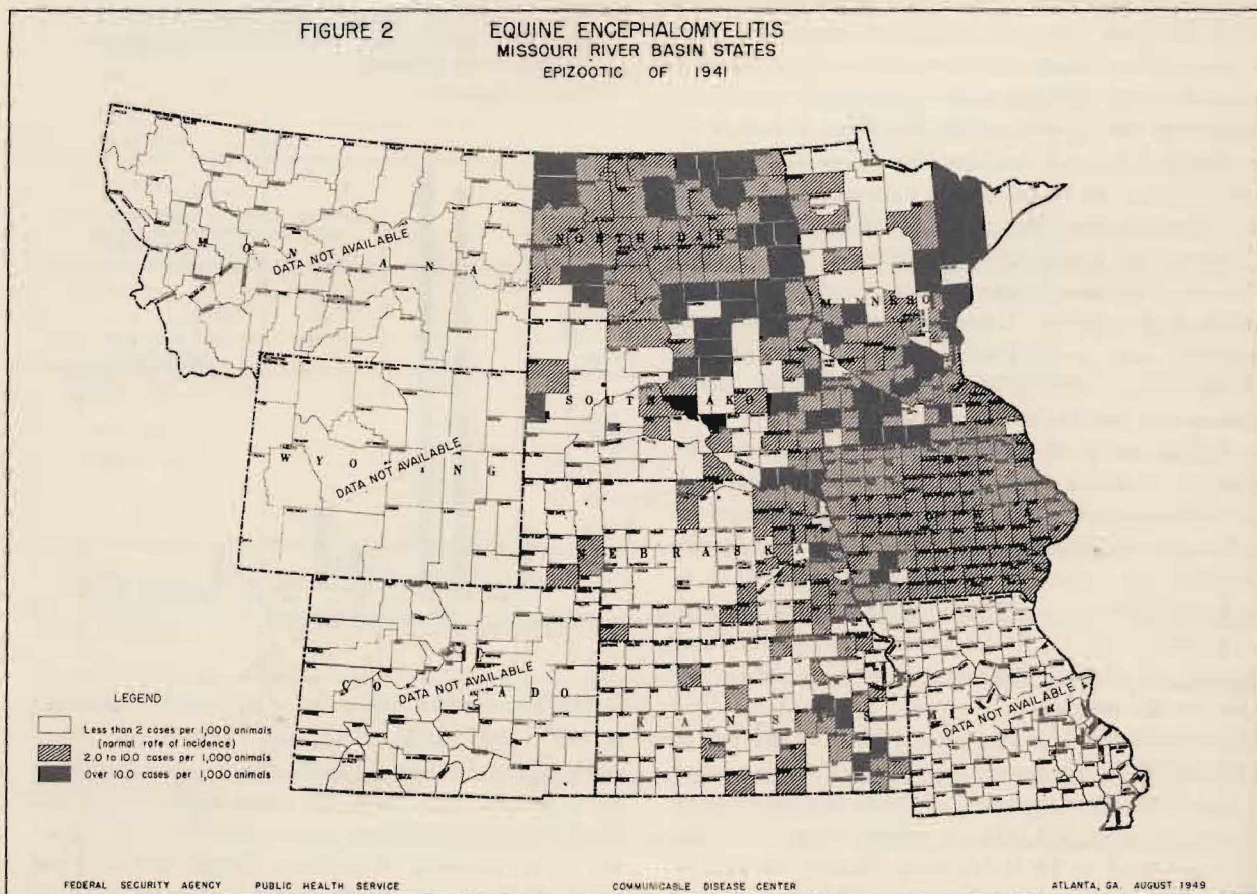


FIGURE 3

EQUINE ENCEPHALOMYELITIS
MISSOURI RIVER BASIN STATES
EPIZOOTIC OF 1944

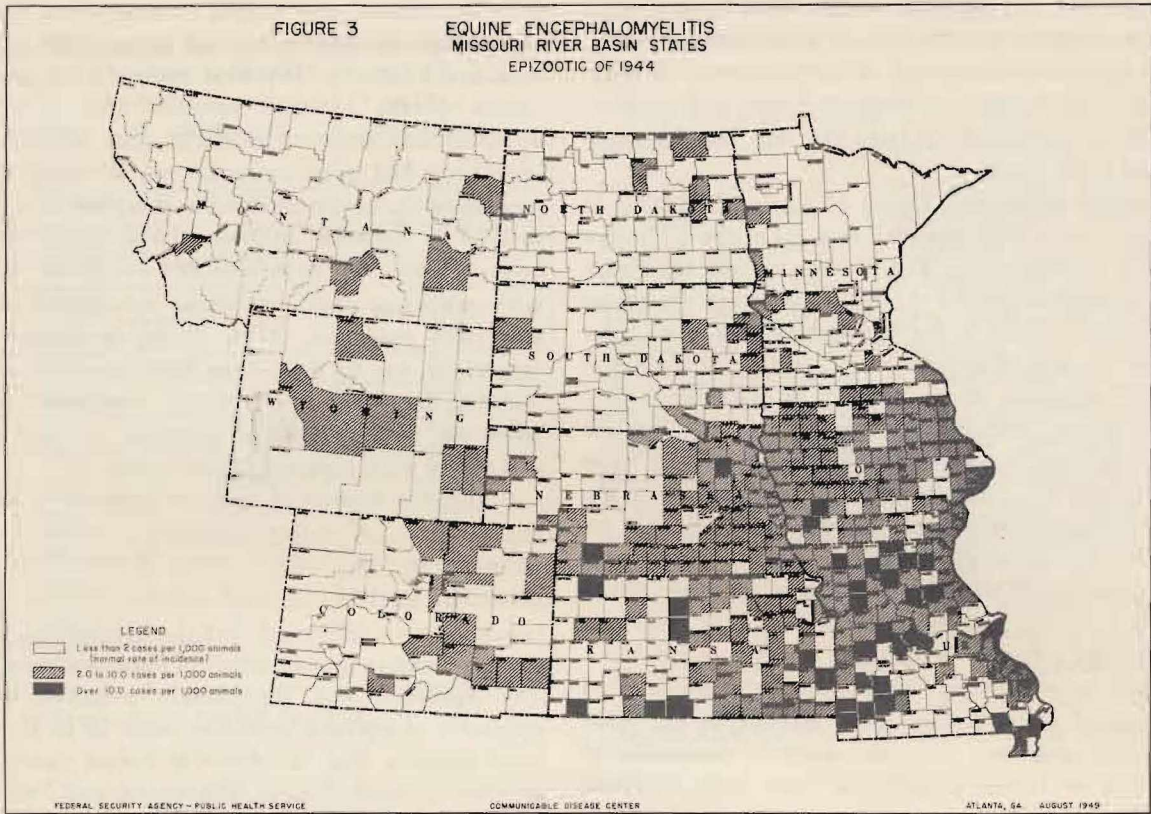
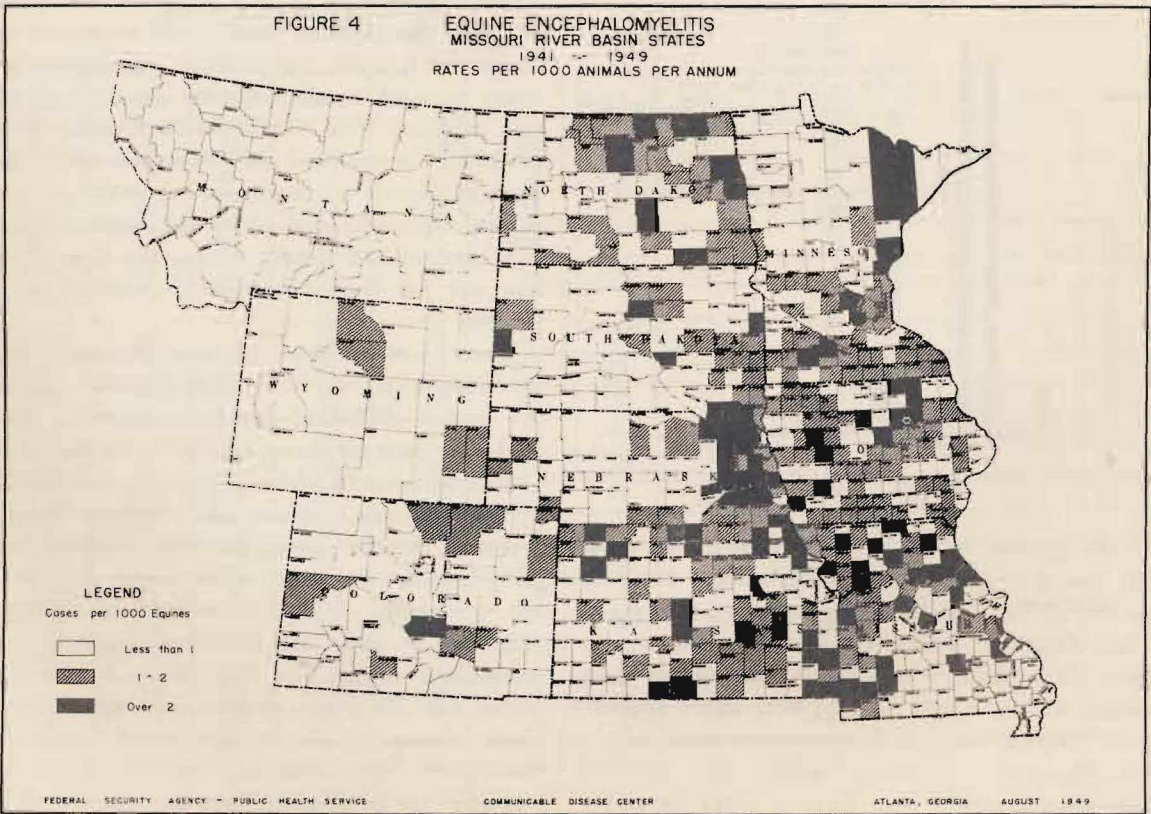


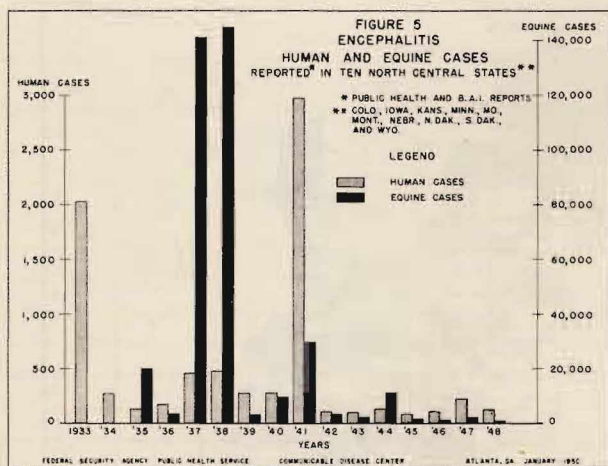
FIGURE 4

EQUINE ENCEPHALOMYELITIS
MISSOURI RIVER BASIN STATES
1941 - 1949
RATES PER 1000 ANIMALS PER ANNUM



period the encephalitis viruses were widely distributed within nine States. In these States, nearly one hundred counties had an average rate of more than 2 infections per 1,000 animals, and in hundreds of additional counties the rate was between 1 and 2 per 1,000.

Human Infections. Cases of encephalitis in humans have been reported from all of the 10 States under consideration. The viruses of both the Western equine strain and the St. Louis strain are known to infect humans in the Midwestern area. As in the case of many diseases, the reporting of encephalitis infections among humans is considered very incomplete. Probably the biggest single reason for this is that positive clinical diagnosis is quite impossible, and that the identification of the particular strain causing an infection can only be made by serological examination. Furthermore, many encephalitic infections have occurred which do not exhibit characteristic serological reactions of known viruses. In spite of these complications which seriously affect adequate reporting, scattered cases of encephalitis occur throughout the Midwestern area each year, and sporadic outbreaks of greater or lesser proportions have been recorded (figure 5).



In the summer of 1933, approximately two thousand human cases of encephalitis were reported from the 10-State area. The major causative agent of this outbreak is now known as the St. Louis strain. The epidemic apparently was centered in St. Louis and St. Louis County, Mo., where approximately eleven hundred cases were reported. In other Missouri localities, nearly two hundred cases were reported from Kansas City; forty-five

from St. Joseph, and roughly a score from Columbia. Cases also were reported from cities in Illinois and Kentucky. Inquiries made during investigation of the outbreak revealed that a similar epidemic had occurred in Paris, Ill., in 1932, but apparently had been unrecognized. Reviews of the records of St. Louis Children's Hospital from 1915 to 1933 by Hartman (38) showed that approximately forty children had been admitted during the period with symptoms similar to those recognized during the 1933 epidemic. It is likely, therefore, that infections due to this virus have occurred in the Midwest for many years. Later manifestations of infection with this virus occurred in 1937 when 338 cases were reported in St. Louis.

During the summer of 1941 an outbreak of human encephalitis, of rather alarming proportions, occurred in the North Central States. This outbreak was centered in North Dakota and Minnesota; investigations indicated that the etiological agent was the Western equine strain of encephalomyelitis. The epidemic was immediately preceded by an epizootic of equines involving some 10 to 15 thousand animals. The incidence of human cases was greatest in North Dakota, Minnesota, and Nebraska which reported 1,100, 669, and 366 cases, respectively.

Within the 10-State area, local outbreaks of undiagnosed types of encephalitis are reported almost every year. A small outbreak involving 11 cases was reported from southwestern Kansas in 1948. In 1949, an outbreak of 69 human infections of Western equine etiology was reported from north central Colorado; and during the same year, about one hundred and twenty cases, the type of which has not yet been determined, occurred in North Dakota.

Records of the reported morbidity and mortality of encephalitis for the 10 Midwestern States for the period 1933-1947 are summarized in table 4. Morbidity data for these States for the period 1930-1948 are shown in table 5. In many years the totals approximate one another, and in three of the years, reported deaths exceeded the reported cases. Allowing for the many difficulties of diagnosis, the probability is that the mortality figures are likely to be more accurate than are those of the morbidity totals. The conclusion is drawn that either the diagnosis or the reporting, or both, in those cases which do not result in death, is inadequate. If a mortality rate of 20 percent in encephalitis is allowed, then the number of cases

TABLE 4

Human Encephalitis in 10 Midwestern States

Year	Total* Morbidity	Total* Mortality
1933	2,047	-
1934	255	169
1935	147	151
1936	173	122
1937	394	265
1938	448	200
1939	268	155
1940	262	109
1941	2,824	404
1942	120	106
1943	97	128
1944	133	88
1945	66	86
1946	78	71
1947	211	87
Total	7,261	2,141

*From Public Health Reports.

must be nearly five times that of the deaths, instead of being approximately equal, as the statistics would indicate.

Infections in Animals Other Than Equines and Humans. There is considerable evidence to indicate that viruses of the arthropod-borne encephalitis may be found in numerous animals other than equines and humans. As indicated in table 1, the Eastern equine strain has been found in one species of mosquito, and one biting louse (*Mallophaga*). The Western equine strain has been found in at least six species of mosquitoes, one assassin-bug (*Triatoma sanguisuga*), and three species of mites. It is important to note that this strain has been found repeatedly in the mosquito, *Culex tarsalis* Coquillette. The St. Louis strain has been found in three species of mosquitoes, and one mite, *Dermanyssus gallinae* (De Geer). The California strain was found in at least two species of mosquitoes. A neurotropic virus of unknown identity was found in the mite, *Liponyssus sylvium* (Canestrini and Fanzago) in California. In Central America, the Venezuelan equine strain was

TABLE 5

Human Encephalitis Cases Reported from 10 Midwestern States*
1930 - 1948

Year	Colo.	Iowa	Kans.	Minn.	Mo.	Mont.	Nebr.	N. Dak.	S. Dak.	Wyo.	Total
1930	9	52	14	38	36	11	10	23	2	1	196
1931	7	40	14	28	2	7	4	10	4	2	118
1932	12	29	9	29	35	10	8	23	3	3	161
1933	14	56	167	68	1,660	10	42	24	4	2	2,047
1934	9	21	61	45	75	5	25	7	2	5	255
1935	8	17	41	31	31	8	7		4		147
1936	40	16	39	23	19	17	7	5	3	4	173
1937	9	15	77	33	190	13	21	7	27	2	394
1938	90	31	40	50	36	72	11	107	9	2	448
1939	37	24	74	14	21	65	8	19	3	3	268
1940	46	38	46	18	10	58	14	24	1	7	262
1941	158	129	69	669	18	91	366	1,100	194	30	2,824
1942	14	13	25	5	6	16	0	27	11	3	120
1943	16	9	32	3	11	2	3	9	6	6	97
1944	24	9	16	9	8	8	0	50	4	5	133
1945	8	5	21	4	7	4	5	11	1	0	66
1946	8	9	19	3	9	2	7	15	0	6	78
1947	14	32	20	13	6	11	19	91	2	3	211
1948	2	19	21	6	4	2	8	34	30	4	130
Total	525	564	805	1,089	2,184	412	565	1,586	310	88	8,128

*From Public Health Reports.

found in the mosquito, *Mansonia tittilans* (Walker). All of these arthropods, except the last, are known to occur in the Midwestern States.

Numerous published reports of serum surveys completed during epidemic and interepidemic periods show that the viruses evidently infect a comparatively large number of species of wild birds, domestic birds, and wild mammals. This is not surprising when the magnitudes of epidemics and epizootics such as occurred in 1937, 1938, and 1941 are considered.

Relatively few published reports are available which indicate the presence or absence of the viruses in animals other than humans and equines in the 10-State area. The Western equine virus has been found in the hog (12), the deer (10), the prairie chicken (10), the assassin-bug (*T. sanguisuga*), and the *C. tarsalis* mosquito (6). Hammon (39) found evidences of the Western equine strain in the chicken, mourning dove, and meadow lark, and of the St. Louis strain in the meadow lark, a woodpecker, a jack rabbit, and the red fox squirrel in Oklahoma in 1944. Extensive surveys of rodents completed by Canadian workers in Saskatchewan and Manitoba (23) have failed to demonstrate any evidence of infection.

EPIDEMIOLOGY

At present, a simple and factual description of the epidemiology of the arthropod-borne encephalitis cannot be given. Although a mass of pertinent facts has been established, certain missing information is needed before coherent and conclusive accounts are possible. Obviously, however, the data at hand permit the formulation of working hypotheses.

One such hypothesis is that blood-sucking mites, parasitic upon birds and domestic fowl, serve as a permanent reservoir of the viruses. The viruses are maintained from year to year by transovarial passage, or in overwintering populations of infected mites. These parasites initially infect their hosts, the birds; but bird-to-bird infection is largely completed by culicine mosquitoes, principally *C. tarsalis*. Repeated isolations of the viruses from culicine mosquitoes, together with successful laboratory transmission studies, quite conclusively implicate these mosquitoes in the maintenance of the infection and possibly its spread to equines and humans. At the moment, *C. tarsalis* appears to be the principal vector; but since naturally infected *Aedes* mosquitoes have been found, and since species of this genus are

often very abundant and attack man and animals in large numbers, their importance as vectors cannot be discounted. The roles played by other biting arthropods cannot be evaluated on the data at present available.

DISCUSSION

It is firmly established that virus encephalitis in both humans and horses is a substantial problem in the 10 States grouped around the Missouri River. Every year a hundred or more deaths are reported, while from time to time severe epidemics appear, affecting thousands of humans, and tens of thousands of horses. The chain of events that leads to this disease is not fully understood, and no feasible methods of prevention are available at present. When an epidemic occurs, little can be done to stop it.

The incidence of encephalitis is probably much greater than would appear from official statistics. This is due to a variety of reasons, the first and most important being that virus encephalitis is extraordinarily difficult to diagnose, except possibly when it occurs in epidemic form. There are a number of organisms which can give rise to the general symptoms of encephalitis, and it is often impossible to distinguish these clinically, whereas for specific virus encephalitis infections, definite diagnosis cannot be made without laboratory assistance of a most specialized nature. In the 10-State area, such laboratory services for routine examination are almost completely lacking; therefore, encephalitis as reported in official statistics includes the epidemiological manifestations of several diseases, and it is impossible to state the relative importance of any specific one.

Another important reason for the inadequate reporting of encephalitis is that practicing physicians generally are not accustomed to contacting public health representatives in their State on such matters. This is partially due to the lack of local health services throughout large areas in many of the States. Furthermore, the distribution of physicians definitely congregated in larger towns leaves large rural areas inadequately supplied with medical attention.

Factors which would greatly improve the reporting of encephalitis as well as other diseases are:

1. Provision of adequate laboratory services, which are available to the general physician, for diagnosis of suspected encephalitis infections.

2. Provisions for the establishment of increased local health services, and closer liaison of these

services with practicing physicians.

3. General recognition by practitioners that it is their responsibility to report notifiable diseases promptly.

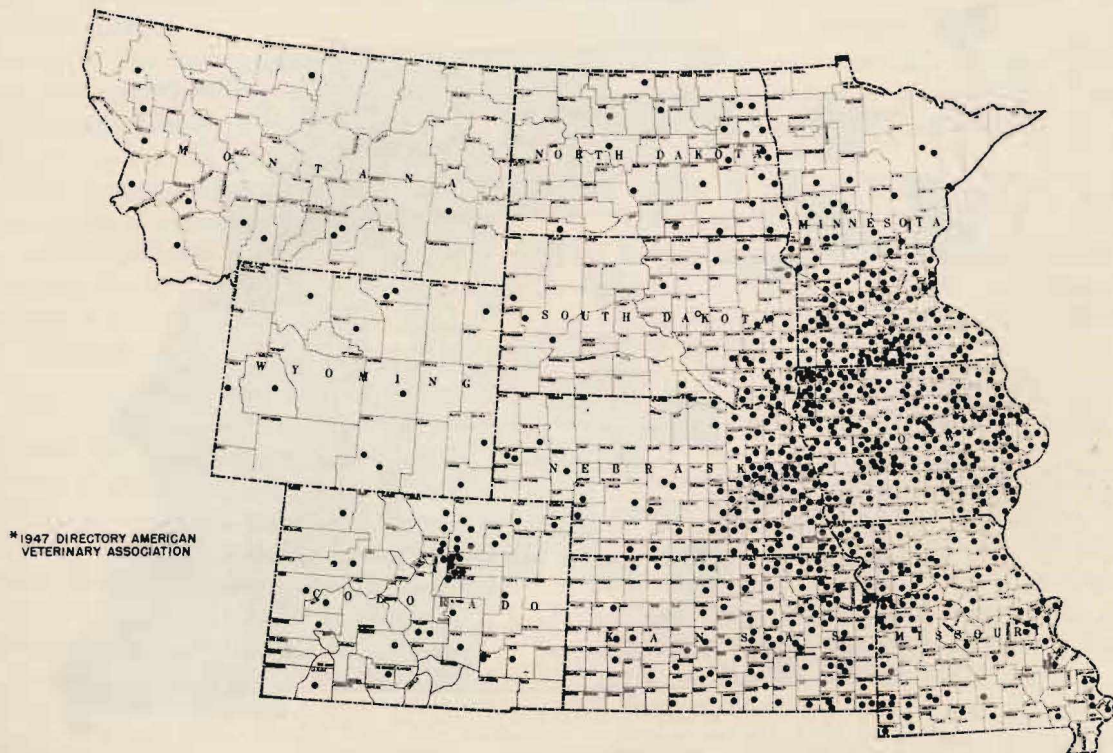
Reporting of equine infections appears to be much more satisfactory than reporting of human infections. In the Midwestern area, where agriculture is the dominant industry, interest in the reporting of equine cases might be expected because of economic reasons. It should be recognized, however, that the distribution of veterinarians is such (figure 6) that there are large areas of the country having substantial horse populations (figure 7) where veterinary services are inadequate, and where little knowledge is available on the incidence of virus infections. Insufficient work has been done on the typing of organisms causing specific infections. Most infections reported are classified provisionally as being of Western equine etiology, whereas in actual fact these assumptions may not be justifiable. Efforts are needed to discover the relative importance of various neurotropic strains which affect equines

in the Midwestern area.

Basic Biological Studies. It is evident that the virus encephalitic infections of humans and horses are only portions of a most complicated ecological process which involves many forms of animal life. Most of the studies which have been made in the past have been concentrated properly around the virus and its recovery from various host animals. It is obvious that the bionomics and interrelationship of many arthropods and animal species, such as birds and mammals, are involved in the perpetuation in nature of these infections. These phenomena are also of prime importance to those public health workers whose job it is to develop adequate control measures. Relatively little is known in the Midwestern area concerning specific biological features of the various animals which are undoubtedly associated with the spread of these infections. Much remains to be done in these respects before the ecology of the viruses can be properly explained, and before practical control methods can be developed. Of primary significance are:

1. The discovery of natural reservoirs of the

FIGURE 6
AREAS SERVED BY PRACTICING VETERINARIANS
MISSOURI RIVER BASIN STATES
1947*



*1947 DIRECTORY AMERICAN
VETERINARY ASSOCIATION

FEDERAL SECURITY AGENCY PUBLIC HEALTH SERVICE COMMUNICABLE DISEASE CENTER ATLANTA, GEORGIA JAN 1950

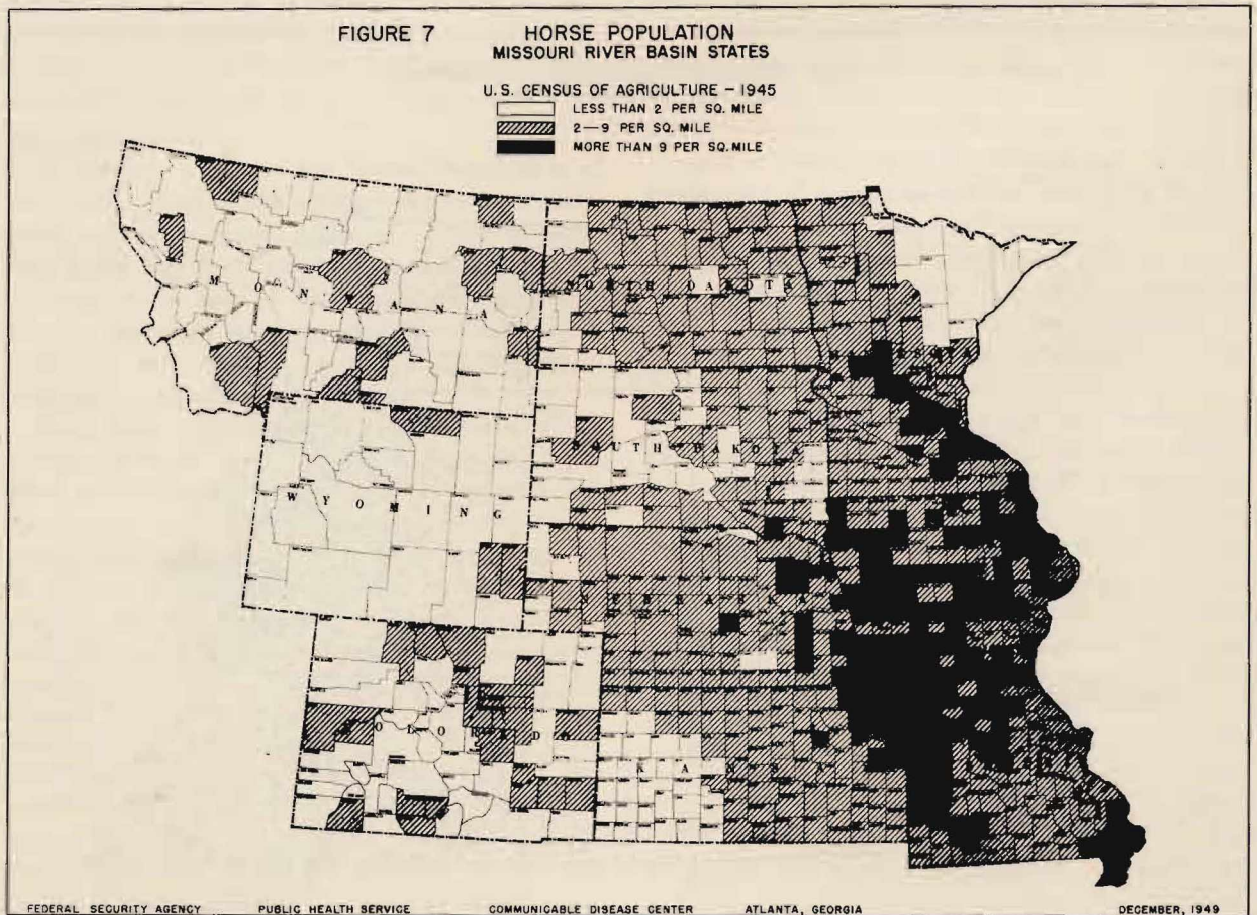
infections and the means by which they are maintained from year to year. If the mite-to-bird association comprises a natural cycle, such matters as taxonomy, physiology, and ecology of the mites, as well as the birds, must be thoroughly explored.

2. Additional evidence which will confirm the role of culicine mosquitoes as vectors is urgently needed, including clarification of the relative importance of the various species. The accumulation of much additional data on the bionomics of mosquitoes inhabiting the Missouri River Basin for this purpose, as well as for formulating possible means of control, is necessary.

3. In view of the close association of equine epizootics and human epidemics, further studies are needed to determine their exact relationship. Should it be that the horse is a necessary host in the chain of transmission of the virus to humans, the decrease in their numbers should be similarly paralleled by a reduction in human cases, and certainly in recent years the number of cases has

shown a steady reduction. If, on the other hand, both horses and humans are in the nature of "dead ends" so far as the life cycle of the virus is concerned, then the smaller number of horses should have little effect upon the human incidence of the disease.

4. An obvious factor common to all outbreaks of encephalitis is that of water. It is water that determines where the maximum populations of people will be found, as well as that of horses, birds, mites, and mosquitoes. The area of maximum incidence of encephalitis in general coincides with that of maximum rainfall; where locations are found outside of this, usually some other source of water such as irrigation is there also. It is likely that transmission of the viruses of encephalitis is dependent upon culicine mosquitoes, and therefore any activity which involves the manipulation of water in which these mosquitoes might breed should include provisions to minimize this possibility. The construction of a large number of dams in the Missouri River Basin and the concu-



rent widespread use of irrigation waters, might well lead to an increase in incidence of the various virus encephalitides, unless appropriate control measures are incorporated in the project during the developmental period.

The Program of Study at Midwestern CDC Services. The primary aim is to assist the various States in their campaigns against infectious diseases. At the moment, this is limited to furnishing advice on the diagnosing of cases, and to consulting on the various epidemics, when such assistance is requested by the State health officers.

Little more than the above can be done until the epidemiology of the disease has been clarified. In the meantime, a full-scale attack is being made

by a well-coordinated team of biologists, working out of Kansas City. Such a problem requires scientists trained in many branches, and the group includes an epidemiologist, a veterinarian, an ornithologist, an acarologist, and many entomologists. Cooperating with these teams are virologists from the University of Kansas Medical School, as well as the CDC Virus and Rickettsia Laboratory at Montgomery, Ala., and the Bureau of Reclamation and other government agencies. Additional specialized consultants are scattered throughout the United States. This encephalitis project covers so many fields of biology that it is only by the teamwork of scientists of many specialties that an answer can be found to the problem.

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